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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/645,077	08/21/2003	Ivan N. Rich	6115-002	6943

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EXAMINER	
GABEL, GAILENE	
ART UNIT	**PAPER NUMBER**
1641	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/645,077	RICH, IVAN N.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *69-135* is/are pending in the application.

4a) Of the above claim(s) *104,105,107-116 and 120-135* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *69-103,106 and 117-119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *69-135* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/10/04; 3/5/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 69-119, with traverse, filed on March 5, 2007, is acknowledged and has been entered. Applicant's further election of the species in claim 106, drawn to proliferation agent including erythropoietin, granulocyte-macrophage colony stimulating hormone (CSF), granulocyte CSF, stem cell factor, interleukin-3 (IL-3), IL-6, and Flt3L, is also acknowledged. Claims 120-135 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being claims drawn to a non-elected invention. Claims 103-105, and 107-116 are also withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being claims drawn to a non-elected species. Currently, claims 69-135 are pending. Claims 69-102, 106, and 117-119 are under examination.

2. Applicant traverses the restriction requirement on the grounds that examination of all claims would not impose serious burden to Examiner as required by proper restriction. Applicant contends that a separate search would not be required for Groups I and II and for the individual species recited in claims 104-116.

In response, Applicant's argument that Groups I and II and the separate distinct species encompassing different inventions, would not require separate searches is not persuasive, because Group I is a system and Group I is a system, each of which have separate and independent requirement for search, examination, and consideration for

patentability. Group II specifically requires functionality which Group I does not. Hence, literature search for each method and system is distinct since the structural requirements of each invention, i.e. a method and a system, are different. While searches would be expected to overlap, there is no reason to expect the searches to be coextensive. As for the species requirement, should applicant traverse on the ground that the species should not be restricted for reasons that they relate and are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Oath/Declaration

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because: it does not identify the mailing address of each inventor. A mailing address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The mailing address should include the ZIP Code designation. The mailing address may be provided in an application data sheet or a supplemental oath or declaration. See 37 CFR 1.63(c) and 37 CFR 1.76.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 69-103, 106, and 117-119 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 69, part b) is indefinite in reciting, "serum mix" because it is unclear what is encompassed in reciting, "mix" which appears to be a term that lacks a comparative basis for defining its metes and bounds. See also part g) and claim 74.

Claim 69, part c) is indefinite in reciting, "methyl-cellulose mix" because it is unclear what is encompassed in reciting, "mix" which appears to be a term that lacks a comparative basis for defining its metes and bounds. See also part g) and claim 76.

Claim 69, part d) is indefinite in reciting, "a mix of growth factors" and "a mix of cytokines" because it is unclear what is encompassed in reciting, "mix" which appears to be a term that lacks a comparative basis for defining its metes and bounds.

Claim 74 is indefinite in reciting, "IMDM." Acronyms and abbreviations should be defined at least one time in a given set of claims.

Claim 77 is confusing in relation to claims 69, 74, and 76, all from which it depends because it is unclear what structural or functional cooperative relationship exists between the (1) methyl cellulose in part b) and that contained in the methyl cellulose mix recited in claim 76, and (2) the fetal bovine serum in part a) and that contained in the serum mix recited in claim 74.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 69-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bell et al. (US 2002/0120098 A1) and in further view of Crouch et al. (The use of ATP Bioluminescence as a measure of Cell Proliferation and Cytotoxicity, Journal of Immunological Methods, 160: 81-88 (1993)).

Bell et al. disclose cell culture systems for stimulation of hematopoietic, i.e. erythropoietic) progenitor cell proliferation. The system comprises a target population of mononuclear cells, a serum mix, a methylcellulose mix, a proliferation agent, a medium, and a plate. The target mononuclear cells are obtained and isolated from bone marrow, umbilical cord blood and peripheral blood from animal tissue of human, primate, cattle, horse, sheep, and swine (see page 6 [0060], page 14 [0120], page 17 [0146]). The target mononuclear cells are enriched and expanded hematopoietic progenitor cells such as burst-forming unit erythroid (BFU-E) cells and colony-forming unit-erythroid (CFU-E) cells. The target mononuclear cells may also be enriched and purified into single hematopoietic stem cells such as colony-forming unit-granulocyte, erythroid, macrophage, megakaryocyte (CFU-GEMM) cells (see page 7 [0071]. The proliferation agent used in the system includes cytokines such as any one of erythropoietin, stem

cell growth factor, interleukin 3 (IL-3), and IL-6 (see page 9 [0082]). The cell populations containing hematopoietic progenitor and stem cells are plated in semi-solid suspensions of methylcellulose, agar, and culture medium containing erythropoietin and optionally, cytokines, stem cell factor, IL-1, IL-3, Flt-3 ligand, and IL-6 to stimulate non-erythroid hematopoietic progenitor cell proliferation (see page 9 [0085]). The culture medium in the system is maintained at an atmospheric concentration of 5% oxygen (see page 11 [0099], [0101]). The culture medium in the system may contain 10% fetal bovine serum. The target population may be plated with Iscoves modified Dulbecco cell culture medium (IMDM) containing 0.8% methyl cellulose (about 0.4% to about 0.7% methyl cellulose), 30% fetal bovine serum (FBS), and 1% bovine serum albumin (BSA). The mononuclear target cell population may also be comprised of differentially distinguishable population of primitive hematopoietic cells as defined by CD34, CD38, and glycophorin A cell surface antigen expression, and which are differentially identified by cell surface marker indicators that bind them such as anti-glycophorin A (see page 12 [0105], [0145], and [015]). Example 9 specifically provides instructions for selectively isolating the differentially distinguishable population of primitive hematopoietic cells defined by CD34 and CD38 cell surface marker expression using magnetic bead separation (STEMSEP^{TM} system or (CEPRATE LC system) and flow cytometry and cell sorting apparatus (FACS: flow activated cell sorting). At Example 11, Bell et al. provide a test compound (Ganciclovir) and instructions for testing its ability to modulate, i.e. inhibit, proliferation or differentiation of the different hematopoietic progenitor cell

populations, as well as analyzing their sensitivities in comparison to a negative standard.

Bell et al. differ from the instant invention in failing to disclose a reagent capable of generating luminescence in the presence of ATP, to thus determine the proliferative state of a target mononuclear cell population.

Crouch et al. disclose a system and instructions for determining the proliferative status (cell proliferation) of a population of primitive (lymphoblastic, promyelocytic) hematopoietic cell population. The hematopoietic cells are granulocyte-macrophage colony-forming cells (GM-CFC) and granulocyte colony-forming cells (G-CFC), i.e. TF-1 and NFS-60 cells, isolated from human peripheral blood, and are detected for cytokine dependent proliferation by stimulation of granulocyte-macrophage colony stimulating factor (GM-CSF) and granulocyte colony stimulating factor (G-CSF) (see Abstract). The hematopoietic cell lines are cultured and maintained in a cell growth culture medium containing 12.5% FBS (fetal calf serum). Crouch et al. specifically teach an ATP reagent which generates luminescence in the presence of ATP in bioluminescence assay. Crouch et al. further teach that when isolated MNCs are combined with luciferin-luciferase monitoring reagent, bioluminescence output is generated and measured (see page 81, column 2 and page 82, columns 1 and 2). The amount of luminescence generated by the reagent indicates the amount of ATP present in the MNC cell population, wherein the amount of ATP indicates the proliferative status of the hematopoietic cells.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the ATP reagent as taught by Crouch that has ability to generate luminescence in the presence of ATP to determine proliferative status of hematopoietic progenitor cells, into the system comprising growth culture medium as taught by Bell for stimulating proliferation of progenitor hematopoietic cells and maintaining the cells, because Bell specifically taught that his culture system including a medium, favors hematopoietic progenitor cell or stem cell growth, expansion, and proliferation upon stimulation, so as to be applicable for assay and testing for transplantation and treatment of hematopoietic disorders, and Crouch's ATP bioluminescence reagent provides accurate and safe measure of proliferation status of the cells so as to enable optimal hematopoietic progenitor cell sample selection and isolation prior to transplantation.

6. Claims 74-102, 106, and 117-119 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bell et al. (US 2002/0120098 A1) and in further view of Crouch et al. (Journal of Immunological Methods, 160: 81-88 (1993)) as applied to claims 69-73 above, and further in view of Tang et al. (US Patent 6,824,973).

Bell et al. and Crouch et al. have been discussed supra. Bell et al. and Crouch et al. differ from the instant invention in failing to teach that the serum mix further comprises insulin and transferrin.

Tang et al. disclose culture systems and methods of promoting hematopoietic stem and progenitor cell proliferation or survival. See column 28, line 63 to column 30, line 29. Specifically, Tang et al. disclose using IMDM culture medium and supplementing it with serum and additives including human serum, horse serum, bovine serum albumin, insulin and transferrin (column 30, lines 1-12).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate insulin and transferrin used in the serum additive mixture of Tang into the system for proliferating and maintaining hematopoietic progenitor cells as taught by Bell and modified by Crouch, because Tang specifically taught application of any one of the additives in the serum mixture with culture media that stimulate and support proliferation of hematopoietic cells, for purposes of testing for proliferative status of hematopoietic progenitor cells such as those taught by Bell and Crouch so as determine their efficacy for transplantation.

7. No claims are allowed.

Remarks

8. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Bauer et al. (US Patent 6,440,407) disclose systems, kits, and instructions for ex vivo expansion of hematopoietic cells using IL-3 multiple mutation polypeptides. Specifically, Bauer et al. disclose a system having hematopoietic progenitor cells

cultured in a tissue culture medium that is prepared by supplementing IMDM with human transferrin in an amount of 100 ug/ml (0.1 nM) (see column 11, line 53 to column 12, line 66; and especially column 15, lines 36-58). In colony assay evaluation, the cells are incorporated into an assay culture tube containing Iscove's based methylcellulose, growth factors, and in an atmosphere of 5% oxygen (see column 19, lines 9-22).

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Z4Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gailene R. Gabel
Patent Examiner
Art Unit 1641
March 31, 2007